REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

I. STATUS OF THE CLAIMS AND FORMAL MATTERS

Claims 4 and 6-8 are pending in this application. Claims 4 and 6-8 have been amended without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

No new matter is added.

Claims 4 and 6-8 have been amended to clarify claim language and correct formatting of claim terms as suggested by the Examiner. Support for the amendments may be found throughout the specification and claims as originally filed. See, in particular, the abstract, page 4, ll. 6-27 and Table 1 of the specification as originally filed.

It is submitted that these claims are in full compliance with the requirements of 35 U.S.C. § 112. The amendments to the claims and the remarks herein are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but rather the amendments and remarks are made simply for clarification and to round out the scope of protection to which the Applicant is entitled.

II. THE OBJECTION TO THE CLAIMS IS OVERCOME

Claims 4 and 6-8 are objected to because of informalities: Claims 4 and 6-8 have been amended in accordance with the Examiner's suggestions and hence all objections are rendered moot.

Reconsideration and withdrawal of the objections to claims 4 and 6-8 are respectfully requested.

III. THE REJECTIONS UNDER 35 U.S.C. § 112 ARE OVERCOME

Claim 6 is rejected under 35 U.S.C. §112, first paragraph, as based on a disclosure which is not enabling. The rejection is traversed.

The Examiner alleges that critical or essential information needed to practice the claimed invention, but not included in the claim(s), is missing and is not enabled by the disclosure.

Applicant submits that claim 6 has been amended to presently recite " The method of claim 4, wherein the coagulation Factor VIII is a von Willebrand Factor (vWF) B domain deleted rFVIII (recombinant Factor VIII).", thereby overcoming the Examiner's rejection. Techniques to arrive at recombinant DNA were known to one of ordinary skill in the art at the time of the invention and following the guidance of the specification with regards to General Recombinant DNA Methodology Techniques, as stated on page 25, ll. 6-19 of the specification as filed, one would be enabled to arrive at the claimed invention.

Claims 4 and 6-8 are rejected under 35 U.S.C. §112, second paragraph, as failing to set forth subject matter, which applicant(s) regard as their invention.

Claim 4 and dependent claims were alleged to lack antecedent basis for the recitation of "...a patient who does not present with anti-coagulation factor VIII antibodies". Claim 4 and 8 have been amended to recite "said patient" thereby overcoming the Examiner's rejection.

Claim 6 was alleged to be indefinite for the recitation of "using recombinant DNA technology" and to lack antecedent basis for the recitation of "the coagulation Factor VIII and IXa reagents". Claim 6 has been amended to overcome the Examiner's rejections for indefiniteness and lack of antecedent basis.

Accordingly, it is respectfully requested that the rejections under 35 U.S.C. §112, first and second paragraph, be reconsidered and withdrawn.

IV. THE REJECTIONS UNDER 35 U.S.C. §103 ARE OVERCOME

Claims 4 and 6-8 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Barrowcliffe et al. (as stated in IDS - Applicant would like to clarify that the reference is Barrowcliffe et al. J Lab Clin Med 1983 Jan; 101(1) 34-43, the only Barrowcliffe reference on file submitted in an IDS on April 29, 2005 and that the arguments that follow are based on this reference; "Barrowcliffe") in view of Lang et al. (U.S. Patent No. 5,506,112; "Lang") taken with Capon et al. (U.S. Patent No. 4,965,199; "Capon"). The rejection is traversed.

The Examiner is respectfully directed to the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. In re Laskowski, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); In re Obukowitz, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). Although a teaching, suggestion, or motivation to combine is no longer rigidly required for a finding of obviousness, it remains the primary guarantor against a non-statutory hindsight analysis. Ortho-McNeil Pharm., Inc. v.

Mylan Labs., Inc., 520 F.3d 1358, 1365 (Fed. Cir. 2008). Further, as stated by the Court in In re Fritch, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." The requirement that for the §103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicant's disclosure. In re Dow, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir. 1988).

Furthermore, The Supreme Court has reaffirmed the factors set out in Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are…ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727.

Applicant respectfully points out that establishing a *prima facie* case of obviousness requires that the prior art reference, or references when combined, teach or suggest all the claim limitations. MPEP 2143. "To establish prima facie obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art." In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Applying the law to the instant facts, the references relied upon by the Examiner does not disclose, suggest or enable the Applicant's invention.

Applicant submits that claim 4 as pending recites "A method of treating Haemophilia A or Haemophilia B, comprising administering by injection to a patient in need thereof an effective amount of a sterile pharmaceutical composition consisting essentially of coagulation Factors VIII and IXa, wherein the coagulation Factor IXa reduces the concentration of coagulation Factor VIII in the composition in comparison to a composition which does not comprise coagulation Factor IXa, and **wherein said patient does not present with anti-coagulation Factor VIII antibodies**." (emphasis added)

Barrowcliffe explains at page 34 that "about 15% of haemophiliac patients develop antibodies to FVIII and their treatment poses a major difficulty". Barrowcliffe goes on to state that the addition of purified Factor IXa and phospholipid could protect Factor VIII from subsequent inactivation by antibody and that the major protective effect was provided by the phospholipid. Barrowcliffe specifically indicates, see last sentence of the abstract, that "the addition of phospholipid to FVIII concentrates could have important clinical applications in the treatment of haemophiliacs **with antibodies to FVIII**" (emphasis added). Barrowcliffe, at best, merely indicates that a combination of FVIII, FIXa and phospholipid may have a protective effect against inactivation of FVIII by antibody. It is important to note that a skilled person would view Haemophilia with anti-FVIII antibodies as distinct from Haemophilia without anti-FVIII antibodies. Therefore, there is no teaching, suggestion or motivation whatsoever in Barrowcliffe for a person of ordinary skill in the art to address a haemophiliac disease state in which Factor VIII antibodies are not present. Applicant reiterates that the claimed invention relates to a method of treating patients **who do not present with Factor VIII antibodies**.

The Examiner also clearly states on page 6 of the Office Action that Barrowcliffe et al. does not *per se* teach treating Haemophilia and Applicant submits that this deficiency cannot be remedied by Lang and Capon.

The present invention is based on the surprising finding that FIXa allows the concentration of FVIII in a composition for treating Haemophilia to be reduced (see for example page 4, ll. 6-8 of the specification as originally filed), This is based on the demonstration that the FIXa concentration is crucially important in determining the clotting process, especially at low FVIII concentrations. This is clearly shown in Figure 3A and discussed at page 6, ll. 10- 24, page 6, l. 28 to page 7, l. 22, page 28, l. 30 to page 29, l. 9 and page 31, ll. 6-10 of the application as originally filed. Thus the present invention teaches a skilled person to treat haemophiliac patients, who do not present with anti-FVIII antibodies, using a lower concentration of FVIII.

Lang and Capon fail to disclose anything more relevant than Barrowcliffe in this regard. In particular, Lang relates only to *in vitro* assays, using a composition comprising a low concentration of factor IXa and other components. This composition is added to a sample to measure factor VIII activity. There is no suggestion whatsoever in Lang that a composition comprising FVIII and FIXa should be used in a therapeutic method to treat a haemophiliac patients lacking anti-FVIII antibodies.

Capon does not teach a method of treating Haemophilia A or Haemophilia B, comprising administering to a patient in need thereof a pharmaceutical composition consisting essentially of coagulation factor VIII and IXa. In particular, there is no teaching at all in Capon that Factor IXa should actually be added to a composition to be used therapeutically to treat a haemophiliac patient who does not have anti-FVIII antibodies.

Capon only suggests that Factor IXa is part of the blood clotting cascade (see Figure 1) and therefore Factor IXa, and the other factors shown, would normally already be present inside an individual. There would, therefore, be no motivation to add Factor IXa to a composition comprising Factor VIII for treating a haemophiliac patient who does not have anti-FVIII antibodies.

Hence, the references provide no guidance at all to arrive at the claimed invention and cannot render the claimed invention obvious. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, an interview with the Examiner and SPE are respectfully requested and the Examiner is additionally requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

In view of the remarks and amendments herewith, the application is in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution.

Respectfully submitted,
VEDDER PRICE P.C.
Attorney for Applicants

By: 

Thomas J. Kowalski
Reg. No. 32,147
Deborah L. Lu, Ph.D.
Reg. No. 50,940
Smitha B. Uthaman, Ph.D.
Reg. No. L0613
Tel. No. (212) 407-7700
Fax No. (212) 407-7799